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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/933,309	08/20/2001	Gregory M. Fahy	FAH02 P-300A	7331

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Suk

Office Action Summary	Application No.	Applicant(s)	
	09/933,309	FAHY, GREGORY M.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-22 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-22 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Status of Application, Amendments and/or Claims

The amendment filed 29 August 2003 has been entered in full. Claims 16-22 and 32-34 are under examination.

The information disclosure statement filed 02 September 2003 was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

The Fahy Declaration under 37 CFR 1.132 filed 29 August 2003 has been entered.

The Examiner has acknowledged that cancellation of non-elected species is not, as yet, required. This is in reference to the objection of claims 20 and 21, as set forth at page 2 of the previous Office Action, 04 March 2003.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection of claims 17-22 under 35 U.S.C. 112, second paragraph, as set forth at pages 3-4 of the previous Office Action (04 April 2003) is *withdrawn* in view of the amendment (29 August 2003).

Claim Rejections - 35 USC § 112, Second Paragraph

Claim 16 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The basis for this rejection is set forth at pages 3-4 of the previous Office Action (04 April 2003).

Applicants state that the Examiner's basis for rejecting claim 16 relies on arguments that confuse the distinction between the requirements of 35 USC 112, first paragraph and 35 USC 112, second paragraph. Applicants state that the Examiner appears to be arguing that the claims are indefinite because they are not enabled.

Applicants' arguments have been fully considered but not found persuasive. The Examiner never used the word "enablement" in the 35 USC 112, second paragraph rejection, so it is unclear why Applicants think the distinction between 112, first paragraph and 112, second paragraph have been confused. The Examiner used a form paragraph (paragraph 7.34.01) to make the instant rejection. Please see MPEP 706.03(d).

Applicants assert that the Examiner has incorrectly stated that the claim is drawn to regenerating the patient's involuted thymus. The claim is directed to a method for transplanting organs and grafting tissue, not a method for regenerating a patient's involuted thymus. Applicants contend that the steps do not comprise injecting the immunological equivalent into the regenerated thymus, "but instead, first, require a step of restoring immune system function by regenerating the patient's involuted thymus". Applicants contend that the Examiner's conclusion that "steps of regenerating the

involuted thymus have not been taught" is incorrect and irrelevant. Applicants state, "as demonstrated by the Examiner's own statements at page 5 of the Office Action, methods of thymus regeneration are known in the art, and thus need not be described by Applicant. Applicants maintain that enablement is immaterial with respect to definiteness and that the correct issue under 35 U.S.C. 112, second paragraph is whether those having ordinary skill in the art would understand the metes and bounds of the invention. Applicants maintain that those having ordinary skill in the art, as is evident from the prior art of record mentioned by the Examiner, would understand the meaning of the expression restoring immune system function by regenerating the patient's involuted thymus. Applicants assert that although it is inappropriate to base a rejection under 35 U.S.C. 112, second paragraph (indefiniteness) on lack of enablement, the prior art of record also demonstrates that those having ordinary skill in the art know how to restore immune system function by regenerating a patient's involuted thymus.

Applicants' arguments have been fully considered but not deemed persuasive. As was stated above, the Examiner is not basing a rejection under 35 USC 112, second paragraph on lack of enablement. Claim 16 is drawn to a method for transplanting organs and grafting tissue into a patient comprising specific steps. One of the steps comprises restoring immune system function by regenerating the patient's involuted thymus. The MPEP states, a claim which fails to interrelate essential elements of the invention as defined by Applicants in the specification may be rejected under 35 USC 112, second paragraph, for failure to point out and distinctly claim the invention (MPEP 2172.01). Regenerating the patient's involuted thymus is part of the steps of the method

claim. Contrary to Applicants' assertion, the steps *do* comprise injecting the immunological equivalent into a regenerated thymus (lines 4-5 of claim 16). The steps recite that immune system function is first restored by regenerating the thymus, and then the immunological equivalent is injected into the regenerated thymus. Furthermore, the Examiner recited references provided by Applicants in the IDS to demonstrate lack of enablement (page 5, last Office Action). The recital of references in the 112, first paragraph rejection has no bearing on the 112, second paragraph rejection of claim 16.

Applicants maintain that it is intentional that the claim does not set forth any steps involved in the method/process (regenerating an involuted thymus). Applicants state that the invention is "a method for transplanting organs and grafting tissue into a patient, " not a method of restoring immune function by regenerating a patient's involuted thymus". Applicants assert that it is not necessary to limit the method of transplanting organs and grafting tissue into a patient by using any particular step of restoring immune system function by regenerating the patient's involuted thymus. Particular techniques for restoring immune function are the subject matter of dependent claims 20-23. Applicants maintain that there is not any statue or rule that authorizes an Examiner to arbitrarily demand that an Applicant incorporate limitations into a claim. More specifically, 35 U.S.C. 112, second paragraph, does not provide any authorization for rejecting claims as being too broad. Applicant has intentionally encompassed methods for transplanting organs using any step of restoring immune system function by regenerating the patient's involuted thymus, injecting the immunological equivalent of the tissue or organ to be transplanted into the patient into the regenerated thymus, and

then transplanting the organ. Accordingly, the requirements of 35 U.S.C. 112, second paragraph have been met.

Applicants' arguments have been fully considered but not deemed persuasive. Applicants state that the invention is a method for transplanting organs and grafting tissue into a patient, not a method of restoring immune function by regenerating a patient's involuted thymus. The Examiner understands that "a method for transplanting organs and grafting tissues" is in the preamble, *however* the steps of the claimed method comprise *both* regenerating a thymus and transplanting organs and grafting tissue. Applicants assert that it is not necessary to limit the method of transplanting organs and grafting tissue into a patient by using any particular step of restoring immune system function by regenerating the patient's involuted thymus and that particular techniques for restoring immune function are the subject matter of dependent claims 20-23. This is incorrect because the thymus must be regenerated before the immunological equivalent can be injected. The claim is indefinite because it fails to set forth the steps involving regenerating the thymus. The omitted steps of regenerating the thymus are essential to the method of claim 16.

Lastly, Applicants contend that there is not any statute or rule that requires an Applicant to define every term that is used in a claim. It is only necessary that those having ordinary skill in the art can understand the metes and bounds of the claims based on the ordinary meanings of the words, and any definitions provided in the specification. Applicants state that "immunologically equivalent" is frequently use in the literature, and means that the immunologically equivalent material induces an

immunological effect equivalent to a specific material, e.g., the tissue or organ to be transplanted into a patient. Applicants assert that the meaning of the expression immunological equivalent is defined in the specification. Applicants state that donor-specific cell or antigens that the immunological equivalent of the tissue itself are materials that stimulate "deletion or anergy of the cells otherwise responsible for later rejecting the transplanted tissue or organ" and include "endogenously-derived sample in the case of those with autoimmune diseases". Applicants cite pages 15, line 24 through page 16, line 4.

Applicants' arguments have been fully considered but not deemed persuasive. The pages Applicants cite specifically state, "at this time, a surgeon skilled at thymic biopsy retrieval injects into the thymus an appropriate sample of the tissue or organ to be transplanted later, or injects any other donor-specific cells or antigens (for example, bone marrow cells) that are the immunological equivalent of the tissue itself in stimulating deletion or anergy of the cells otherwise responsible for rejecting the transplanted tissue or organ. This tissue may be an endogenously-derived sample in the case of those with autoimmune disease". The specification uses "immunological equivalent" in a sentence but fails to specifically teach the definition of "immunological equivalent". The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 112, First Paragraph

Claims 16-22 and 32-34 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is set forth at pages 4-7 of the previous Office Action (04 April 2003).

Applicants state that the Examiner's statements demonstrate that regeneration of involuted thymus is well known in the art but takes the position that regeneration of a patient's involuted thymus does not necessarily result in restoration of immune system function. Applicants discuss the McCormick, Goff and Perico references. Applicants submit more references.

Applicants' arguments have been fully considered but not deemed persuasive. The claimed invention is drawn to a method comprising (1) restoring immune function by regenerating the patient's involuted thymus (2) injecting the immunological equivalent of the tissue or organ to be transplanted into the regenerated thymus of the patient (3) transplanting said organ or grafting said tissue. Using the references of record, the Examiner merely stated the drawbacks, side effects and complications associated with regenerating a thymus. As is apparent from the new references submitted by Applicant, there are many conflicting views regarding thymus regeneration.

Applicants argue that the Examiner stated the instant specification fails to demonstrate that a patient can have an involuted thymus regenerated. Applicants

contend that it is necessary only that the instant specification describes a method whereby an involuted thymus can be regenerated if the method is followed. Applicants assert that a working Example of the efficacy of the Fahy art for the induction of thymic regeneration is appended in the declaration of the inventor. Applicants contend that if intrathymic injection is possible in rats in dogs, it is reasonable to assume it is possible in humans and that it is well known in the art that humans can undergo an organ transplant or tissue graft. Applicants maintain that the fact that the intrathymic transplant method works in species as diverse as rats and dogs, puts the burden of proof on the proposition that it cannot work in man. Applicants argue that anyone of ordinary skill in the art would be moved to assume that the Applicant's method would be successful and useful in human subjects.

Applicants' arguments have been considered but are not found persuasive. As was stated above, the claimed invention is drawn to a method comprising (1) restoring immune function by regenerating the patient's involuted thymus (2) injecting the immunological equivalent of the tissue or organ to be transplanted into the regenerated thymus of the patient (3) transplanting said organ or grafting said tissue. Regenerating a thymus *in laboratory animals* is known in the art. Intrathymic injection *in laboratory animals* is known in the art. The combination of intrathymic injection and transplantation of organs and grafting of tissue *in laboratory animals* is known in the art. Transplantation of organs and grafting tissue *in humans and laboratory animals* is known in the art. The instant invention, however, *comprises the entire steps*. Applicants appear to be arguing enablement by taking apart the different steps of the invention,

then using references to support the enablement for each step. The novelty of the invention is based on the entire method steps occurring in humans, not just the parts. The specification states that intrathymic injection and subsequent transplantation requires a functioning thymus (page 2, line 19-page 3, line 21). The specification attempts to demonstrate that tolerance (organ transplant and tissue grafting) can be increased by restoring immune system function by regenerating the thymus in the presence of human growth factor and DEAH, in addition to intrathymic injection in humans.

The Fahy Declaration under 37 CFR 1.132 filed 29 August 2003 is insufficient to overcome the rejection of claims 16-22 and 32-34 based upon 35 USC 112, first paragraph, enablement as set forth in the last Office action. The Fahy declaration states that in response to hGH and DHEA, the percent increase in total thymic lymphoid (functional) mass was 92%. However, as was stated by Goff (reference cited in the last Office Action), a change (or lack of change) in thymic morphology does not prove increased or decreased thymic function; immunological or endocrine function must be assessed. The Fahy Declaration fails to disclose the insulin levels, which are increased in the presence of hGH but drop in the presence of DHEA. In addition, the Fahy Declaration fails to demonstrate that immune system function has been restored. "Restoration of immune system function" is a limitation of the claim. Both the Fahy Declaration and the specification fail to teach intrathymic injection in humans. The specification fails to teach "restoring immune system function by regenerating the

patients involuted thymus". The submitted references fail to teach intrathymic injection in humans.

Applicants state that the fact that the disclosure does not provide immunological or endocrine assays does not mean that the disclosure is not enabling. Applicants contend that intrathymic injection is known in the art and it is not a purpose of the invention to teach what is already known in the art. Applicants maintain that the fact that human thymic biopsies and animal intrathymic injection methods are known in the art implies that similar methods can be used in man and would be a trivial point for any thoraic surgeon. Applicants maintain that transplanting an organ or grafting of tissue are well known in the art and do not require working examples. Applicants maintain that the factors cited by the Examiner such as rejection, side effects, complications were unavoidable considered in the specification and have been solved in the cited prior art available at the time the invention was made or are illusory.

Applicants' arguments have been considered but are not found persuasive. As was stated above, restoring immune system function is a limitation of the claim which the specification fails to demonstrate. The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. Lack of a working example, however is a factor to be considered, especially in a case involving an unpredictable and undeveloped art. Intrathymic injection *in humans* is not known in the art. As was stated above, various steps of the claimed method are known in the art for laboratory animals. Transplanting organs and tissue grafting of tissue are well known in

the art for human and laboratory. However, the instant invention, is based on the entire method steps in a human. The assertion is that increased tolerance of transplants and/or grafts can occur by regenerating a thymus in addition to intrathymic injection in humans.

Undue experimentation is a conclusion reached by weighing all of the wands factor. If one skilled in the art can readily anticipate the effect, than there is predictability in the art. In this case, the art (for the claimed invention) is either unpredictable or unknown based on the evidence provided. The evidence for the degree of predictability in the art also relates to the amount of direction needed in the specification. The specification provides little guidance and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. A considerable amount of time is permissible for the quantity of experimentation needed to make or use the invention based on the disclosure. However this depends on if the invention is routine or if the skilled artisan is given sufficient direction or guidance. In the instant case, the experimentation is not routine and Applicant has provided little or no guidance. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on 9:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RMD
January 7, 2004

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